

CLAIMS:

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1. A method of producing a library of mutant nucleic acid molecules comprising:
- (a) obtaining a template nucleic acid;
- (b) preparing a first oligonucleotide corresponding to a first desired
5 mutation within said template nucleic acid;
- (c) preparing a second oligonucleotide corresponding to a second desired
mutation within said template nucleic acid;
- (d) mixing the oligonucleotides prepared in said steps (b) and (c) so as to
hybridize said oligonucleotides to said template nucleic acid;
- 10 (e) subjecting the mixture of step (d) to the linear cyclic amplification
reaction to produce a library of mutant template nucleic acids.
2. The method according to claim 1, wherein said oligonucleotides in said steps
(b) and (c) are discontinuous.
3. The method according to claim 1, wherein said step first and second
15 oligonucleotides are present in less than saturation concentration.
4. The method according to claim 1, wherein the mixture of said step (d) further
comprises non-mutagenic oligonucleotides corresponding to either or both of said
first and second oligonucleotides.
5. The method according to claim 1, wherein said template nucleic acid
20 corresponds to a desired protein product.
6. The method according to claim 4, wherein said protein product comprises an
enzyme, hormone, vaccine, peptide therapeutic or antibody.
7. The method according to claim 4, further comprising the steps of:
- (f) transforming said mutant template nucleic acids from said library into
25 a competent host cell;
- (g) expressing protein corresponding to said mutant nucleic acids in said
host cell;
- (h) screening said expressed proteins for desired characteristics.
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8. A method for producing a library of mutant nucleic acid molecules comprising the steps of:

- (a) obtaining a template nucleic acid;
- (b) preparing two or more primers corresponding to the template nucleic acid, wherein at least one primer is in opposite orientation to the remaining primers and at least one primer is a mutagenic primer corresponding to a desired mutation;
- (c) mixing the primers in said step (b) so as to hybridize said primers to said template nucleic acid; and
- (d) subjecting the mixture of step (c) to the linear cyclic amplification reaction to produce a library of mutant template nucleic acids.

9. The method of claim 8, wherein said two or more primers comprises 3 to 15 primers or 4 to 7 primers.

10. The method of claim 8, wherein said primers in said step (b) are discontinuous.

11. The method according to claim 8, wherein said primers in step (b) are present in less than saturation concentration.

12. The method of claim 8, wherein all said primers in step (b) are mutagenic primers.

13. The method of claim 8, wherein said at least one mutagenic primer comprises 1 to 12 nucleotide mutations.

14. The method of claim 8, wherein said at least one mutagenic primer encodes 1 to 4 amino acid mutations.

15. The method according to claim 8, wherein said template nucleic acid corresponds to a desired protein product.

16. The method according to claim 15, wherein said protein product comprises an enzyme, hormone, vaccine, peptide therapeutic or antibody.

17. The method according to claim 8, further comprising the steps of:

- (e) transforming said mutant template nucleic acids from said library into a competent host cell;

- (f) expressing protein corresponding to said mutant nucleic acids in said host cell; and
- (g) screening said expressed proteins for desired characteristics.

52066224.1/23623-7073